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Aspects of the Microglia Transcriptome

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Aspects of the Microglia Transcriptome

Microglia Information Converted to RNA-Seq Outputs
Generates Laborious Integrative Analyses.

Marissa Lisa Dubbelaar

Most research described in this PhD dissertation was conducted at the Biomedical Sciences of Cells and Systems, Department Moleculair Neuroscience, University Medical Center Groningen, University of Groningen, the Netherlands.

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university of
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Aspects of the Microglia Transcriptome

Microglia Information Converted to RNA-Seq Outputs
Generates Laborious Integrative Analyses

PhD thesis

to obtain the degree of PhD at the
University of Groningen
on the authority of the
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the decision by the College of Deans.

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Table of contents

Abbreviations		8
Chapter 1	General introduction and thesis outline	16
Chapter 2	The kaleidoscope of microglial phenotypes	40
Chapter 3	The effect of post mortem delay on the microglia transcriptome	74
Chapter 4	Microglia meta-analysis: A comparative approach to profile the macaque microglial transcriptome of multiple organisms	88
Chapter 5	BRAIn Interactive Sequencing Analysis Tool; facilitating interactive transcriptome analyses	108
Chapter 6	Summary and general discussion	126
Chapter 7	Nederlandse samenvatting / Dutch summary	136
Chapter 8	References	142
	Appendices	
	I Acknowledgements	172
	II Curriculum vitae	178

Abbreviations

General

Term	Fullname
3' UTR	3' untranslated region
A β	amyloid beta
AD	Alzheimer's disease
ALS	Amyotrophic lateral sclerosis
API	application programming interface
ASC	apoptosis-associated speck-like proteins containing a caspase recruitment domain
ATAC	assay for transposase accessible chromatin
ATP	adenosine triphosphate
BG	basal ganglia
BRAIN-SAT	brain interactive sequencing analysis tool
CA1	<i>cornu Ammonis</i> 1
CARD	caspase recruitment domain
ChIP	chromatin immunoprecipitation
CNS	central nervous system
CPM	count per million
DAFS	data-adaptive flag method for RNA-Seq data
DAM	disease-associated microglia
DAMP	damage-associated molecular pattern
DEA	differential expression analysis
DNA	deoxyribonucleic acid
E7.5	embryonic day 7.5
E8.5	embryonic day 8.5
EAE	experimental autoimmune encephalomyelitis
EdU	5-Ethynyl-2'-deoxyuridine
EMP	erythro-myeloid progenitor
ENA	european nucleotide archive
EOAD	early-onset Alzheimer's disease
ETS	expressed sequencing tags
FACS	fluorescence-activated cell sorting
FC	fold change
FDR	false discovery rate
GEO	gene expression omnibus
GF	germ-free
GO	gene ontology
GOAD	glia open access database
GWAS	genome-wide association studies
HGP	human genome project
IdU	5-iodo-2'-deoxyuridine
LOAD	late-onset AD

LPM	large peritoneal macrophages
LPS	lipopolysaccharides
M1	classical activation
M2	alternative activation
MDI	microglia developmental index
MGnD	microglial neurodegenerative/-toxic
MHC	major histocompatibility complex
miRNA	micro ribonucleic acid
MO	myelinating oligodendrocytes
MOG	myelin-oligodendrocyte-glycoprotein peptide
MOLGENIS	molecular genetics information systems
mRNA	messenger ribonucleic acid
MS	Multiple sclerosis
NAc	nucleus accumbens
NFO	newly formed oligodendrocytes
ORF	open reading frame
P9	postnatal day 9
PAMP	pathogen-associated molecular pattern
PCA	principal component analysis
PCR	polymerase chain reaction
PD	Parkinson's disease
PLAC-seq	proximity ligation-assisted ChIP-Seq
PMD	post-mortem delay
pol II	ribonucleic acid polymerase II
PTM	posttranslational modifications
QEA	quantitative expression analysis
RA	retinoic acid
REST	representational state transfer
RNA	ribonucleic acid
RNA-Seq	ribonucleic acid sequencing
RT	room temperature
scRNA-Seq	single-cell RNA sequencing
SNc	substantia nigra pars compacta
SPF	specific pathogen-free
SPM	small peritoneal macrophages
SRA	sequencing read archive
ST	spatial transcriptomics
TBP	TATA-binding proteins
TF	transcription factor
TLR	toll-like receptor
TPM	transcript per million
tSNE	t-distributed stochastic neighbor embedding
UMI	unique molecular identifier
VTA	ventral tegmental area

Gene names

Symbol	Name	Synonyms
<i>ADGRG1</i>	adhesion G protein-coupled receptor G1	<i>GPR56, TM7LN4, TM7XN1</i>
<i>ALDH1L1</i>	aldehyde dehydrogenase 1 family member L1	<i>FTHFD, 10-FTHF</i>
<i>ALOX5AP</i>	arachidonate 5-lipoxygenase activating protein	<i>FLAP</i>
<i>ANK1</i>	ankyrin 1	<i>ANK, SPH1</i>
<i>ANKRD39</i>	ankyrin repeat domain 39	<i>MGC41816</i>
<i>APLP2</i>	amyloid beta precursor like protein 2	<i>APPL2, APPH</i>
<i>APOC1</i>	apolipoprotein C1	
<i>APOE</i>	apolipoprotein E	<i>AD2</i>
<i>APP</i>	amyloid beta precursor protein	<i>AD1</i>
<i>ATF3</i>	activating transcription factor 3	
<i>AXL</i>	AXL receptor tyrosine kinase	<i>UFO, JTK11, Tyro7, ARK</i>
<i>B2M</i>	beta-2-microglobulin	
<i>BBS10</i>	Bardet-Biedl syndrome 10	<i>C12orf58, FLJ23560</i>
<i>BIN1</i>	bridging integrator 1	<i>AMPHL, SH3P9, AMPH2</i>
<i>C1QA</i>	complement C1q A chain	
<i>C1QB</i>	complement C1q B chain	
<i>C1QC</i>	complement C1q C chain	<i>C1QG</i>
<i>C3</i>	complement C3	<i>CPAMD1, ARMD9, C3a, C3b</i>
<i>C4A</i>	complement C4A (Rodgers blood group)	<i>CPAMD2, C4S, C04, C4, C4A3, C4A2, C4A4, C4A6, C4B, RG</i>
<i>C5AR1</i>	complement C5a receptor 1	<i>C5R1, C5A, C5AR, CD88</i>
<i>CABLES1</i>	Cdk5 and Abl enzyme substrate 1	<i>HsT2563, FLJ35924</i>
<i>CCL2</i>	C-C motif chemokine ligand 2	<i>SCYA2, MCP1, MCP-1, MCAF, SMC-CF, GDCF-2, HC11, MGC9434</i>
<i>CCL3</i>	C-C motif chemokine ligand 3	<i>SCYA3, G0S19-1, LD78ALPHA, MIP-1-alpha</i>
<i>CCL4</i>	C-C motif chemokine ligand 4	<i>LAG1, SCYA4, MIP-1-beta, Act-2, AT744.1</i>
<i>CCL5</i>	C-C motif chemokine ligand 5	<i>D17S136E, SCYA5, RANTES, SISd, TCP228, MGC17164</i>
<i>CCR2</i>	C-C motif chemokine receptor 2	<i>CMKBR2, CC-CKR-2, CKR2, MCP-1-R, CD192, FLJ78302</i>
<i>CCR5</i>	C-C motif chemokine receptor 5	<i>CMKBR5, CKR-5, CC-CKR-5, CKR5, CD195, IDDM22</i>
<i>CCR6</i>	C-C motif chemokine receptor 6	<i>STRL22, CKR-L3, GPR-CY4, CMKBR6, GPR29, DRY-6, DCR2, BN-1, CD196</i>
<i>CD14</i>	CD14 molecule	
<i>CD34</i>	CD34 molecule	
<i>CD40</i>	CD40 molecule	<i>TNFRSF5, p50, Bp50</i>
<i>CD44</i>	CD44 molecule (Indian blood group)	<i>MIC4, MDU2, MDU3, IN, MC56, Pgp1, CD44R, HCELL, CSPG8</i>
<i>CD52</i>	CD52 molecule	<i>CDW52, HE5, EDDM5</i>
<i>CD58</i>	CD58 molecule	<i>LFA3</i>
<i>CD68</i>	CD68 molecule	<i>SCARD1, macroiallin, GP110, DKFZp686M18236, LAMP4</i>

CD86	CD86 molecule	CD28LG2, B7.2, B7-2
CD9	CD9 molecule	MIC3, BA2, P24, TSPAN29, MRP-1
CIR1	corepressor interacting with RBPJ, CIR1	CIR
CKB	creatine kinase B	CKBB
CLECT7A	C-type lectin domain containing 7A	CLECSF12, <i>dectin-1</i> , <i>hDectin-1</i> , CD369, SCARE2
COMT	catechol-O-methyltransferase	
CRYBB1	crystallin beta B1	
CSF1	colony stimulating factor 1	M-CSF, MCSF, MGC31930
CSF1R	colony stimulating factor 1 receptor	FMS, C-FMS, CSFR, CD115
CST7	cystatin F	
CTSB	cathepsin B	
CTSD	cathepsin D	CPSD, CLN10
CTSZ	cathepsin Z	CTSX
CX3CR1	C-X-C motif chemokine receptor 1	GPR13, CMKBRL1, CMKDR1, V28, CCRL1
CXCL10	C-X-C motif chemokine ligand 10	INP10, SCYB10, IFI10, IP-10, <i>arg-2</i> , <i>mob-1</i> , C7, <i>gIP-10</i>
CXCL16	C-X-C motif chemokine ligand 16	SR-PSOX, CXCLG16, SRPSOX
CXCR2	C-X-C motif chemokine receptor 2	IL8RB, CMKAR2, CD182
CXCR4	C-X-C motif chemokine receptor 4	LESTR, NPY3R, HM89, NPY3R, D2S201E, <i>fusin</i> , HSY3RR, NPYR, CD184
CYTB	mitochondrially encoded cytochrome b	MTCYB, COB, CYTB, UQCR3
DAB2	DAB adaptor protein 2	DOC-2
DNAJB5	DnaJ heat shock protein family (Hsp40) member B5	Hsc40
DOCK8	dedicator of cytokinesis 8	FLJ00026, FLJ00152, ZIR8, FLJ00346
DPY30	dpy-30 histone methyltransferase complex regulatory subunit	Saf19, HDPY-30, Cps25
EEF1B2	eukaryotic translation elongation factor 1 beta 2	
EGR1	early growth response 1	TIS8, G0S30, NGFI-A, KROX-24, ZIF-268, AT225, ZNF225
ENTPDP1	ectonucleoside triphosphate diphosphohydrolase 1	CD39, NTPDase-1, ATPDase, SPG64
Epb4.112	erythrocyte protein band 4.1-like 2	
ERAP2	endoplasmic reticulum aminopeptidase 2	L-RAP, LRAP
ERCC1	ERCC excision repair 1, endonuclease non-catalytic subunit	RAD10
F11R	F11 receptor	JAM1, PAM-1, JCAM, JAM-1, JAM-A, JAMA, CD321
FCAR	Fc fragment of IgA receptor	CD89
FFAR2	free fatty acid receptor 2	GPR43, FFA2R
FKBP3	FKBP prolyl isomerase 3	FKBP-25, PPIase
FOS	Fos proto-oncogene, AP-1 transcription factor subunit	<i>c-fos</i> , AP-1
FSCN1	fascin actin-bundling protein 1	SNL, p55, FLJ38511
GAS7	growth arrest specific 7	KIAA0394, MGC1348
GNA13	G protein subunit alpha 13	G13, MGC46138
GNLY	granulysin	LAG2, NKG5, LAG-2, D2S69E, TLA519
GOLPH3L	golgi phosphoprotein 3 like	GPP34R
GPR34	G protein-coupled receptor 34	
GPR84	G protein-coupled receptor 84	EX33

<i>GRN</i>	granulin precursor	<i>PCDGF, PGRN, CLN11</i>
<i>GUSB</i>	glucuronidase beta	
<i>H2-D1</i>	histocompatibility 2, D region locus 1	
<i>H2-K1</i>	histocompatibility 2, K1, K region	
<i>HEXB</i>	hexosaminidase subunit beta	
<i>HIF1A</i>	hypoxia inducible factor 1 subunit alpha	<i>MOP1, HIF-1alpha, PASD8, HIF1, bHLHe78</i>
<i>HLA-B</i>	major histocompatibility complex, class I, B	<i>AS</i>
<i>HLA-DRA</i>	major histocompatibility complex, class II, DR alpha	<i>HLA-DRA1</i>
<i>HPRT1</i>	hypoxanthine phosphoribosyltransferase 1	<i>HPRT, HGPRT</i>
<i>IGF1</i>	insulin like growth factor 1	<i>IGF1A, IGF1, IGF-1, IGF</i>
<i>IKBIP</i>	IKBKB interacting protein	<i>FLJ31051, IKIP</i>
<i>IL13</i>	interleukin 13	<i>P600, IL-13, ALRH, BHR1, MGC116786, MGC116788, MGC116789</i>
<i>IL1B</i>	interleukin 1 beta	<i>IL1F2, IL-1B, IL1-BETA</i>
<i>IL1R2</i>	interleukin 1 receptor type 2	<i>IL1RB, CD121b</i>
<i>IL4</i>	interleukin 4	<i>BSF1, IL-4, BCGF1, BCGF-1, MGC79402</i>
<i>IL6</i>	interleukin 6	<i>IFNB2, IL-6, BSF2, HGF, HSF</i>
<i>IRF1</i>	interferon regulatory factor 1	<i>MAR</i>
<i>IRF8</i>	interferon regulatory factor 8	<i>ICSBP1, IRF-8, ICSBP</i>
<i>IRGM</i>	immunity related GTPase M	<i>IRGM1, LRG47, LRG-47, IFI1</i>
<i>ITGAM</i>	integrin subunit alpha M	<i>CR3A, CD11B, MAC-1, CD11b</i>
<i>ITGAX</i>	integrin subunit alpha X	<i>CD11C, CD11c</i>
<i>LGALS3</i>	galectin 3	<i>LGALS2, MAC-2, GALIG</i>
<i>LGALS3BP</i>	galectin 3 binding protein	<i>MAC-2-BP, 90K, BTBD17B, TANGO10B, M2BP, gp90, CyCAP</i>
<i>LGMN</i>	legumain	<i>PRSC1, LGMN1</i>
<i>LPL</i>	lipoprotein lipase	<i>LIPD</i>
<i>LTC4S</i>	leukotriene C4 synthase	<i>MGC33147</i>
<i>MAEA</i>	macrophage erythroblast attacher, E3 ubiquitin ligase	<i>EMP, GID9</i>
<i>MAFB</i>	MAF bZIP transcription factor B	<i>KRML</i>
<i>MAP3K7</i>	mitogen-activated protein kinase kinase kinase 7	<i>TAK1, MEKK7</i>
<i>MCM5</i>	minichromosome maintenance complex component 5	<i>CDC46</i>
<i>MEF2A</i>	myocyte enhancer factor 2A	<i>RSRFC4, RSRFC9</i>
<i>MERTK</i>	MER proto-oncogene, tyrosine kinase	<i>mer, RP38, c-Eyk, Tyro12</i>
<i>MPZL1</i>	myelin protein zero like 1	<i>PZR, FLJ21047</i>
<i>MRC1</i>	mannose receptor C-type 1	<i>MRC1L1, CLEC13D, CD206, bA541I19.1, CLEC13DL</i>
<i>MRC2</i>	mannose receptor C type 2	<i>KIAA0709, ENDO180, CLEC13E, CD280</i>
<i>MRPS36</i>	mitochondrial ribosomal protein S36	<i>DC47, MRP-S36</i>
<i>MYO18A</i>	myosin XVIIIa	<i>KIAA0216, MysPDZ</i>
<i>ND1</i>	mitochondrially encoded NADH:ubiquinone oxidoreductase core subunit 1	<i>MTND1</i>
<i>NFKB2</i>	nuclear factor kappa B subunit 2	<i>LYT-10, p52, p105, NF-kB2, p49/p100</i>
<i>NPC2</i>	NPC intracellular cholesterol transporter 2	<i>HE1, NP-C2, EDDM1</i>
<i>NR2C2</i>	nuclear receptor subfamily 2 group C member 2	<i>TR4, TAK1, TR2R1, hTAK1</i>

<i>NT5DC3</i>	5'-nucleotidase domain containing 3	<i>TU12B1-TY, FLJ11266</i>
<i>NTSR1</i>	neurotensin receptor 1	<i>NTR</i>
<i>OLFML3</i>	olfactomedin like 3	<i>HNOEL-iso, OLF44</i>
<i>P2RY12</i>	purinergic receptor P2Y12	<i>P2Y12, SP1999, HORK3</i>
<i>P2RY13</i>	purinergic receptor P2Y13	<i>GPR94, GPR86, FKSG77, P2Y13</i>
<i>P2RY6</i>	pyrimidinergic receptor P2Y6	<i>P2Y6</i>
<i>PDGFA</i>	platelet derived growth factor subunit A	<i>PDGF1, PDGF-A</i>
<i>PDGFB</i>	platelet derived growth factor subunit B	<i>SIS, SSV</i>
<i>PIK3C2B</i>	phosphatidylinositol-4-phosphate 3-kinase catalytic subunit type 2 beta	<i>C2-PI3K, PI3K-C2beta</i>
<i>PLD3</i>	phospholipase D family member 3	<i>HU-K4</i>
<i>PMEPA1</i>	prostate transmembrane protein, androgen induced 1	<i>TMEPAI, STAG1</i>
<i>PROS1</i>	protein S	<i>PROS</i>
<i>PSAT1</i>	phosphoserine aminotransferase 1	<i>PSA</i>
<i>PSEN1</i>	presenilin 1	<i>AD3, FAD, S182, PS1</i>
<i>PSEN2</i>	presenilin 2	<i>AD4, AD3L, STM2, PS2</i>
<i>PSTPIP1</i>	proline-serine-threonine phosphatase interacting protein 1	<i>PSTPIP, CD2BP1L, CD2BP1, CD2BP1S, H-PIP, PAPAS</i>
<i>PTPRC</i>	protein tyrosine phosphatase receptor type C	<i>CD45, LCA, T200, GP180</i>
<i>PYCARD</i>	PYD and CARD domain containing	<i>TMS-1, CARD5, ASC</i>
<i>RARA</i>	retinoic acid receptor alpha	<i>RAR, NR1B1</i>
<i>RARB</i>	retinoic acid receptor beta	<i>HAP, NR1B2, RRB2</i>
<i>RELA</i>	RELA proto-oncogene, NF-kB subunit	<i>NFKB3, p65</i>
<i>RHOB</i>	ras homolog family member B	<i>ARH6, ARHB, RhoB, RHOH6, MST081</i>
<i>RNF7</i>	ring finger protein 7	<i>SAG, ROC2, CKBBP1</i>
<i>RPL41</i>	ribosomal protein L41	<i>L41</i>
<i>RPS23</i>	ribosomal protein S23	<i>S23, uS12</i>
<i>S100A12</i>	S100 calcium binding protein A12	<i>p6, MRP6, CGRP, CAAF1, CAGC, ENRAGE</i>
<i>SAG</i>	S-antigen visual arrestin	<i>ARRESTIN, RP47</i>
<i>SALL1</i>	spalt like transcription factor 1	<i>TBS, Hsal1, ZNF794</i>
<i>SALL3</i>	spalt like transcription factor 3	<i>ZNF796</i>
<i>SEMA7A</i>	semaphorin 7A (John Milton Hagen blood group)	<i>SEMAL, H-Sema-L, CD108</i>
<i>SEPSECS</i>	Sep (O-phosphoserine) tRNA:Sec (selenocysteine) tRNA synthase	<i>SLA/LP, SLA</i>
<i>SERPINE2</i>	serpin family E member 2	<i>PI7, PN1, GDN, PNI, nexin</i>
<i>Siglech</i>	sialic acid binding Ig-like lectin H	
<i>SLA</i>	Src like adaptor	<i>SLA1, SLAP-1, hSLAP, SLAP</i>
<i>SLCO2B1</i>	solute carrier organic anion transporter family member 2B1	<i>SLC21A9, OATP-B, OATP2B1</i>
<i>SMAD1</i>	glycyl-tRNA synthetase 1	<i>MADH1, MADR1, JV4-1</i>
<i>SMAD1</i>	SMAD family member 1	<i>NA, SMURF2</i>
<i>SMURF2</i>	SMAD specific E3 ubiquitin protein ligase 2	<i>ALS, ALS1, IPOA</i>
<i>SOD1</i>	superoxide dismutase 1	<i>C11orf32, gp250, LR11, LRP9, SorLA, SorLA-1</i>
<i>SORL1</i>	sortilin related receptor 1	<i>NA, SOX4</i>
<i>SOX4</i>	SRY-box transcription factor 4	<i>ON</i>

<i>SPARC</i>	secreted protein acidic and cysteine rich	<i>PU.1, SPI-A, OF, SFPI1, SPI-1</i>
<i>SPI1</i>	Spi-1 proto-oncogene	<i>APRF</i>
<i>STAT3</i>	signal transducer and activator of transcription 3	<i>PJS, LKB1</i>
<i>STK11</i>	serine/threonine kinase 11	<i>hUNC18, MUNC18-1, UNC18, rbSec1</i>
<i>STXBP1</i>	syntaxin binding protein 1	<i>C1orf9, CH1, SLP1, OPT</i>
<i>SUCO</i>	SUN domain containing ossification factor	<i>SLP1, SYTL1</i>
<i>SYNGR1</i>	synaptogyrin 1	
<i>TGFA</i>	transforming growth factor alpha	<i>TGFB, DPD1, CED, TGFbeta</i>
<i>TGFB1</i>	transforming growth factor beta 1	<i>MSSE, ESS1, ALK-5, ACVRLK4, ALK5, TBRI, TBR-i</i>
<i>TGFBRI</i>	transforming growth factor beta receptor 1	<i>MFS2, TBRII, TBR-ii</i>
<i>TGFBRI2</i>	transforming growth factor beta receptor 2	<i>CTMP</i>
<i>THEM4</i>	thioesterase superfamily member 4	
<i>TLR7</i>	toll like receptor 7	
<i>TMEM119</i>	transmembrane protein 119	
<i>TMEM173</i>	stimulator of interferon response cGAMP interactor 1	<i>FLJ38577, NET23, ERIS, MPYS, STING, MITA</i>
<i>TNF</i>	tumor necrosis factor	<i>TNFA, TNFSF2, DIF, TNF-alpha</i>
<i>TPT1</i>	tumor protein, translationally-controlled 1	<i>TCTP, fortilin</i>
<i>TREM2</i>	triggering receptor expressed on myeloid cells 2	<i>TREM-2, Trem2a, Trem2b, Trem2c</i>
<i>TYROBP</i>	transmembrane immune signaling adaptor TYROBP	<i>PLOSL, DAP12, PLO-SL, KARAP</i>
<i>VGLL4</i>	vestigial like family member 4	<i>KIAA0121</i>
<i>VSIR</i>	V-set immunoregulatory receptor	<i>C10orf54, SISP1, GI24, B7-H5, B7H5, VISTA, PD-1H</i>
